REMARKS

Claims 1 and 58 to 97 are pending in this application.[1] Claims 1 and 97 are independent. Favorable reconsideration and further examination is respectfully requested.

Initially, claims 79, 81, 82, and 88 were rejected for allegedly being indefinite. In particular, the Office Action states the following:

> Claim 79, 81-82, and 88 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
>
> Regarding claims 79 and 81-82, the word "means" is preceded by the word(s) "the transducer comprises" in an attempt to use a "means" clause to recite a claim element as a means for performing a specified function. However, since no function is specified by the word(s) preceding "means," it is impossible to determine the equivalents of the element, as required by 35 U.S.C. 112, sixth paragraph. See *Ex parte Klumb*, 159 USPQ 694 (Bd. App. 1967).
>
> Regarding claim 88, the word "means" is preceded by the word(s) "the transducer include" in an attempt to use a "means" clause to recite a claim element as a means for performing a specified function. However, since no function is specified by the word(s) preceding "means," it is impossible to determine the equivalents of the element, as required by 35 U.S.C. 112, sixth paragraph. See *Ex parte Klumb*, 159 USPQ 694 (Bd. App. 1967).

We disagree with the substance of the rejection, since it is perfectly acceptable to claim an element as a "means for...." without an adjective preceding the word "means". For example, MPEP §2181(I) states the following: "(B) "printing means" and "means for printing"...would

[1] The Examiner is urged to independently confirm this recitation of the pending claims.

have the same connotations. Ex parte Klumb, 159 USPQ 694 (Bd. App. 1967)".[2] In our original claims, we have chosen the latter ("means for printing") construction. Nevertheless, in order to advance prosecution, adjectives have been added to the "means for" elements of claims 79, 81, 82 and 88. Withdrawal of the indefiniteness rejection is therefore respectfully requested.

Independent claim 1 was rejected over WO99/30135 (Bahatt). Independent claim 97 was rejected over a combination of Bahatt and U.S. Patent No. 6,159,681 (Zebala). We respectfully traverse these rejections for at least the reasons explained below.

Independent claim 1 is reproduced below:

> 1. An apparatus for detecting a variation in a probe, comprising:
> a sensor comprising a substrate and a plurality of thin film probe structures attached to a surface of the substrate, <u>each probe structure being adapted to undergo a thermoelastic response when excited by temporally varying electromagnetic radiation</u>, the <u>thermoelastic response</u> being a function of physical and/or chemical properties of the probe structure and a sample material binding thereto;
> a source of electromagnetic radiation;
> means for directing the electromagnetic radiation at each probe structure of the sensor; and
> a transducer adapted to <u>determine a thermoelastic response</u> of each probe structure.

The applied art is not understood to disclose or to suggest at least the underlined portions of claim 1 above. The Office Action, however, states the following in its rejection of claim 1.

[2] This statement is just before §2181(II)

> Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by W.O. 99/30135 (BAHATT et al.).
>
> Claim 1 recites an apparatus for detecting a variation in a probe comprising a sensor having a substrate and thin film probe structures, an electromagnetic radiation source, a means of directing radiation, and a transducer. BAHATT et al. discloses an optical resonance system having a sensor means and illumination means in the Abstract. The illuminations device has a lens system for projecting illumination (Abstract) and a light source (page 15, paragraph 2). A substrate having sites for sensing generated resonances is disclosed in page 13, paragraph 7. A sensor means in the form of a transducer having sensor sites for binding unique molecules is disclosed in page 40, paragraph 4 to page 41, paragraph 1; these sensing sites are the same as the probe structures recited in instant claim 1.

We respectfully disagree, and assert that Bhatt is completely silent regarding a thermoelastic response in a probe structure. In fact, Bhatt describes a surface plasmon resonance device, of the type distinguished in the background section of our application. In particular, the background section of our application states the following:

> [0006] <u>Surface plasmon resonance (SPR)</u> is based on an optical phenomenon that occurs in a thin metal film at an optical interface under conditions of total internal reflection. Conventional SPR sensors use a prism `device` coated with a single thin metal layer. Any chemical adsorption to the outer surface of the metal layer or to an immobilised antibody or ligand on the outer surface of the metal layer leads to interfacial changes in the refractive index of the film. By directing a light beam into the prism, it is possible to measure the reflected light as a function of intensity and angle, to produce the well known SPR resonance spectrum. In a recent extension of this concept (U.S. Pat. No. 6,373,577) planar waveguide elements coated with a thin metal film are organised as a linear array of elements in which SPR can be separately generated.
>
> [0007] The present invention is directed to an improved system and apparatus for analysing a sample using one, or an array, of probes that does not require the use of markers, <u>that does not involve SPR</u>, and that can readily be implemented using low cost equipment. <u>In contrast to SPR, the present invention is based on a high peak power beam of electromagnetic radiation which temporarily illuminates a small region of a thermoresponsive sensor, such as a thin metal layer</u>. The incident angle of the beam is constant and the electromagnetic radiation induces a thermal response that can be detected with an appropriate transducer. Chemical adsorption to the surface

> modulates the thermal response, which in turn affects the electrical output of the transducer. (emphasis added)

Surface plasmon resonance, as described in Bhatt, constitutes an excitation of electrons in a metal surface resulting from incident light. Bhatt, however, is completely silent regarding a thermoelastic response in probe structures. Nor are the systems described in Bhatt understood to be adaptable for determining a thermoelastic response. In fact, in its rejection of claim 1, the Office Action does not even appear to address the claimed thermoelastic response or a determination thereof. Zebala is likewise deficient.

In this regard, the Office Action relies on the following passages from Bhatt for their alleged disclosure of the elements of claim 1.

Illumination system

Source

The source is constructed as shown in Figure 3, a two dimensional array of sources 110. The choice of light source is based on the wavelength region required and the etendue (solid angle X pupil area) of the optical system. In the case of SPR, the sensor resonance becomes sharper with increasing source wavelength. The advantage of having narrow resonance is in the ability to detect smaller shifts (sensitivity). On the other hand, the resonance decay length increases with wavelength and thus the reaction site dimensions have to increase (spatial resolution, and system throughput). There is a large variety of broadband or monochromatic sources to choose from, such as: incandescent, LED's, super luminescent diodes, lasers (fixed and tunable, diode, SS, gas), Gas discharge lamps (line and continuum), with or without filters. Incoherent sources are preferred in order to eliminate speckle noise. An example of a light source in this embodiment is a Hewlett-Packard HSDL-4400 LED emitting at 875nm, where the resonance width is 0.3degrees or 5nm. At this wavelength the SPR decay length is of the order of 25 microns. When an array of LED's is used, and placed at the focal plane of the angle-scanning lens system as shown in Figure 1, 40 each LED corresponds to a different angle of illumination. A spacing of 0.395mm between the LED's in the array corresponds to an angular resolution of 0.3deg at f=75mm, and 0.038deg at f=600mm. An array length of 35mm corresponds to a total angle of 26deg at f=75mm, and 3.3deg at f=600mm. This range of angle step and angle range allows for both low resolution/large coverage and high resolution/small coverage scanning. [3]

The invention is further directed toward an anamorphic optical design that allows the analysis system to generate and detect resonances, from a one dimensional array of sites on the same substrate, simultaneously. [4]

[3] Page 15, paragraph 2
[4] Page 13, paragraph 7

Sampling site layout/isolation

Determining sample site configuration is dependent in part on the application. A transducer consisting of a single site is the simplest configuration, however, the most flexible configuration is the array. This is where the transducer is divided up into n x n sites. Each site capable of binding a unique molecule or acting as a control. The advantage of this configuration is the large number of sites that can be produced. For example an array 100 x 100 site gives you 10,000 possible interactive sites in a 1cm sq. [5]

area. Each site provides for different types of chemistries. For example: 1. Compounds that recognize the same molecule but in a different mode (site) can be used to assign higher confidence to the detection method. 2. Different lots of the same compound can be used to assure quality of the chip.3. Some of the site can be used a control sites for chemistry as well as hardware. This type of microscale controls can eliminate more expensive engineering and production steps by being able to eliminate artifacts due to things like transducer warpage, uneven sample introduction temperature control and etc. Linear arrays can also be used but their usefulness as compared to 2D arrays is limited. To help separate the sensor sites on the transducer from other adjacent sensor sites dikes may be used. Dikes are defined as fine line of material that encircles the active sites. These materials could vary depending on the function. For example a high photo adsorbent material could be used to prevent the resonance from propagating into adjacent sites. These dike material could also have hydrophobic properties to facilitate laying down the active surface (prevent run over to adjacent sites). [6]

We do not see anywhere in these paragraphs (or the remainders of Bhatt and Zebala for that matter) where a description of a thermoelastic response or determination thereof is provided. Should the Examiner believe differently, he is respectfully requested to point out specifically where, in Bhatt or Zebala, a thermoelastic response or determination thereof is disclosed or suggested. Absent that, withdrawal of the rejection of claim 1 is respectfully requested.

Independent claim 97 is reproduced below.

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[5] Page 40, paragraph 4
[6] Page 41, paragraph 1

97. (Previously Presented) A method of using an apparatus,
wherein the apparatus comprises:

a sensor comprising a substrate and a plurality of thin film probe structures attached to a surface of the substrate, each probe structure being adapted to undergo a thermoelastic response when excited by temporally varying electromagnetic radiation, the thermoelastic response being a function of physical and/or chemical properties of the probe structure and a sample material binding thereto;

a source of electromagnetic radiation;

means for directing the electromagnetic radiation at each probe structure of the sensor; and

a transducer adapted to determine a thermoelastic response of each probe structure; and

wherein the method comprises:

providing a plurality of probe materials respectively attached to the plurality of thin film probe structures;

exposing the thin film probe structures to a sample material to permit binding of material to surfaces of the thin film probe structures;

using the source of electromagnetic radiation to direct electromagnetic energy at the thin film probe structures; and

detecting changes in thermoelastic response of each thin film probe structure to the electromagnetic energy by comparing a thermoelastic response with and without exposure to the sample material.

For at least the same reasons explained above with respect to claim 1, the applied art is not understood to disclose or to suggest at least the underlined portions of claim 97 above. Accordingly, withdrawal of the rejection of claim 97 is respectfully requested

Dependent claims are also believed to define patentable features. Each dependent claim partakes of the novelty of its corresponding independent claim and, as such, each has not been discussed specifically herein.

It is believed that all of the pending claims have been addressed. However, the absence of a reply to a specific rejection, issue or comment does not signify agreement with or concession of that rejection, issue or comment. In addition, because the arguments made above may not be exhaustive, there may be reasons for patentability of any or all pending claims (or other claims) that have not been expressed. Finally, nothing in this paper should be construed as

an intent to concede any issue with regard to any claim, except as specifically stated in this paper, and the amendment of any claim does not necessarily signify concession of unpatentability of the claim prior to its amendment.

In view of the foregoing amendments and remarks, we respectfully submit that the application is in condition for allowance, and such action is respectfully requested at the Examiner's earliest convenience.

The undersigned attorney can be reached at the address shown below. All telephone calls should be directed to the undersigned at 617-521-7896.

Please apply any fees or credits due in this case to Deposit Account 06-1050 referencing Attorney Docket No. 19002-002US1.

Respectfully submitted,

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